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Health and Environmental Effects Profile for Brominated Dibenzo-p-Dioxins

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16. ABSTRACT

The Health and Environmental Effects Profile for brominated dibenzo-p-dioxins was prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste and Emergency Response to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA) and to provide health-related limits for emergency actions under Section 101 of the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA). Both published literature and information obtained from Agency program office files were evaluated as they pertained to potential human health, aquatic life and environmental effects of hazardous waste constituents.

Quantitative estimates have been presented provided sufficient data are available. Existing data are insufficient to determine an Acceptable Daily Intake (ADI) or a carcinogenic potency factor for brominated dibenzo-p-dioxins.

The Reportable Quantity (RQ) value of 1, 10, 100, 1000 or 5000 pounds is used to determine the quantity of a hazardous substance for which notification is required in the event of a relase as specified by CERCLA based on chronic toxicity. Existing data are insufficient to determine an RQ value.

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HEALTH AND ENVIRONMENTAL EFFECTS PROFILE FOR BROMINATED DIBENZO-p-DIOXINS

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PREFACE

Health and Environmental Effects Profiles (HEEPs) are prepared for the Office of Solid Waste and Emergency Response by the Office of Health and Environmental Assessment. The HEEPs are intended to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA), as well as to provide health-related limits for emergency actions under Section 101 of the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA). Both published literature and information obtained from Agency program office files are evaluated as they pertain to potential human health, aquatic life and environmental effects of hazardous waste constituents. The literature searched and the dates of the searches are included in the section titled "Appendix: Literature Searched." The literature search material is current through November, 1984.

Quantitative estimates are presented provided sufficient data are available. For systemic toxicants, these include Acceptable Daily Intakes (ADIs) for chronic exposures. An ADI is defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect. In the case of suspected carcinogens, ADIs are not estimated in this document series. Instead, a carcinogenic potency factor of q_1^* (U.S. EPA, 1980) is provided. These potency estimates are derived for both oral and inhalation exposures where possible. In addition, unit risk estimates for air and drinking water are presented based on inhalation and oral data, respectively.

Reportable quantities (RQs) based on both chronic toxicity and carcinogenicity are derived. The RQ is used to determine the quantity of a hazardous substance for which notification is required in the event of a release as specified under CERCLA. These two RQs (chronic toxicity and carcinogenicity) represent two of six scores developed (the remaining four reflect ignitability, reactivity, aquatic toxicity and acute mammalian toxicity).

The first draft of this document was prepared by Syracuse Research Corporation under EPA Contract No. 68-03-3228. The document was subsequently revised after reviews by staff within the Office of Health and Environmental Assessment: Carcinogen Assessment Group, Reproductive Effects Assessment Group, Exposure Assessment Group, and the Environmental Criteria and Assessment Office in Cincinnati.

The HEEPs will become part of the EPA RCRA and CERCLA dockets.

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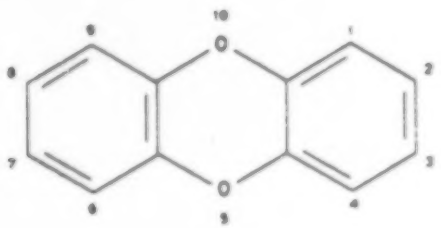
LIST OF ABBREVIATIONS

ADI	Acceptable daily intake
AHH	Aryl hydrocarbon hydroxylase
AIC	Acceptable intake chronic
AIS	Acceptable intake subchronic
BCF	Bioconcentration factor
bw	Body weight
CAS	Chemical Analysis Service
DNA	Deoxyribonucleic acid
FEL	Frank-effect level
i.p.	Intraperitoneal
LD_{50}	Dose lethal to 50% of recipients
LOAEL	Lowest-observed-adverse-effect level
LOEL	Lowest-observed-effect level
MED	Minimum effective dose
NOAEL	No-observed-adverse-effect level
NOEL	No-observed-effect level
ppb	Parts per billion
ppm	Parts per million
RQ	Reportable quantity
TCDD	Tetrachlorodibenzo-p-dioxin

1. INTRODUCTION

1.1. STRUCTURE AND CAS NUMBER

Brominated dibenzo-p-dioxins are a class of compounds having bromine substitution at different benzene ring positions of the dibenzo-p-dioxin nucleus. The accepted system of numbering substituents to the dibenzo-p-dioxin nucleus is as follows:



For mono- to octabromosubstituted dibenzo-p-dioxins, a total of 75 congeners are structually possible; however, data for only a few of these congeners were available in the literature cited in the Appendix. The structure, name, molecular formula, molecular weight and the CAS Registry numbers of eight of these congeners are given in Table 1-1.

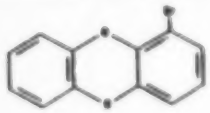
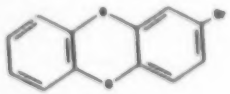
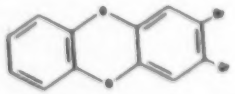
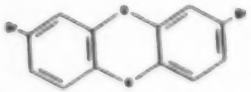
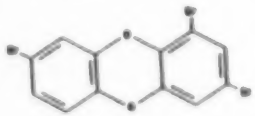
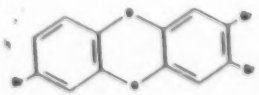
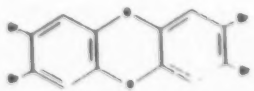
1.2. PHYSICAL AND CHEMICAL PROPERTIES

The physical and chemical properties of the brominated dibenzo-p-dioxins have not been well studied. The scant information available on their physical properties are listed in Table 1-2.

The 2,3,7,8-tetrabromo derivative was found to be insoluble in almost all common organic solvents (Gilman and Dietrich, 1957). Physical properties other than those given in Table 1-2 such as water solubility and K_{ow} are not available in the literature as cited in the appendix. In the absence of experimental data, estimates have been used to derive some of these useful parameters.

TABLE 1-1

Basic Structural Properties and CAS Registry Numbers of a few Brominated Dibenzo-p-dioxins

Structure	Name	Molecular Formula	Molecular Weight	CAS Registry Number
	1-Bromodibenzo-p-dioxin	$C_{12}H_7O_2Br$	262.96	NR
	2-Bromodibenzo-p-dioxin	$C_{12}H_7O_2Br$	262.96	NR
	2,3-Dibromodibenzo-p-dioxin	$C_{12}H_6O_2Br_2$	341.85	50585-37-0
	2,7-Dibromodibenzo-p-dioxin	$C_{12}H_6O_2Br_2$	341.85	NR
	2,8-Dibromodibenzo-p-dioxin	$C_{12}H_6O_2Br_2$	341.85	NR
	1,3,8-Tribromodibenzo-p-dioxin	$C_{12}H_5O_2Br_3$	420.75	80246-33-9
	2,3,7-Tribromodibenzo-p-dioxin	$C_{12}H_5O_2Br_3$	420.75	51974-40-4
	2,3,7,8-Tetrabromodibenzo-p-dioxin	$C_{12}H_4O_2Br_4$	499.65	50585-41-6

NR = Not reported

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TABLE 1-2

Physical Properties of Selected Brominated Dibenzo-p-dioxin

Brominated Compound	Appearance	Solubility in Solvent(s)	Melting Point (°C)	λ max[a] in Chloroform (nm)	Reference
1-Bromo-	white needles	ethyl ether and methanol	104-106	NR	Gilman and Dietrich, 1957
2-Bromo-	NR	ethanol	93-94.5	NR	Gilman and Dietrich, 1957
2,3-Dibromo-	colorless solid	isoctane	157.5-158	308 (3900)[b]	Kende et al., 1974; Kende and Wade, 1973
2,7-Dibromo-	white needles	glacial acetic acid	174-176	NR	Gilman and Dietrich, 1957
2,8-Dibromo-	NR	ethanol	149.5-151	NR	Gilman and Dietrich, 1957
2,3,7,8-Tetrabromo-	white granular	hot pyridine, anisole	334-336	308	Gilman and Dietrich, 1957; Kende et al., 1974; Kende and Wade, 1973

[a]This is the wavelength of maximum absorption.

[b]The extinction coefficient.

NR = Not reported

1.2.1. Estimation Methods.

1.2.1.1. OCTANOL-WATER PARTITION COEFFICIENT (K_{ow}) -- The predictive theory used to derive the K_{ow} is Leo's Fragment Constant Method. A U.S. EPA on-line computer with the GEMS and CLOGP (calculated log P) has been used to derive the K_{ow} values. Three representative brominated compounds, 2,3-dibromo-, 2,8-dibromo-, and 2,3,7,8-tetrabromodibenzo-p-dioxin are used for the derivation of K_{ow} values. The rationale for the selection of the two isomeric dibromo compounds is to demonstrate whether the predictive theories, in the case of such isomeric compounds, have the capabilities to predict different values for each individual parameter. The 2,3,7,8-tetrabromo compound is selected for further environmental impact study because the compound is important with regard to its effects on health. The estimated log K_{ow} values of the three compounds are 6.802, 6.802 and 8.532, respectively. The limitation of the predictive theory in providing different estimated K_{ow} values for the two isomeric compounds is obvious.

1.2.1.2. WATER SOLUBILITY -- The aqueous solubilities of the three selected compounds have been estimated from the above estimated K_{ow} values and the following regression equation (Lyman et al., 1982):

$$\log S = -0.88 \log K_{ow} - 0.01 t_m - 0.012 \qquad (1\text{-}1)$$

S is the aqueous solubility in mol/ℓ, and t_m is the melting point of the compound in °C. The justifications for using this equation rather than several other correlation equations (Lyman et al., 1982) are as follows: this equation is applicable for polyaromatic hydrocarbons; the equation has a high correlation coefficient for the compounds tested; and it uses one of the variable parameters (t_m) for which experimental values are available, providing more realistic solubility values.

Using Equation 1-1 in combination with the t_m values given in Table 1-2 and the estimated K_{ow} values given in Section 1.2.1.1. result in the aqueous solubility values of 9, 11, and 0.01 ppb for 2,3-dibromo-, 2,8-dibromo and 2,3,7,8-tetrabromodibenzo-p-dioxin, respectively.

1.2.1.3. **SOIL PARTITION COEFFICIENT STANDARDIZED WITH RESPECT TO SOIL ORGANIC MATTER CONTENT (K_{oc})** -- The K_{oc} values for the three compounds have been estimated from the following regression equation (Lyman et al., 1982):

$$\log K_{oc} = 0.937 \log K_{ow} - 0.006 \qquad (1\text{-}2)$$

A limitation of this equation is its inability to predict different K_{oc} values for isomeric compounds or compounds with identical K_{ow} values. Using the estimated values for log K_{ow} given in Section 1.2.1.1., log K_{oc} values of 6.37, 6.37 and 7.99 have been estimated for 2,3-dibromo-, 2,8-dibromo- and 2,3,7,8-tetrabromodibenzo-pdioxin, respectively.

1.2.1.4. **BIOCONCENTRATION FACTOR (BCF)** -- The BCF factors have been estimated from the regression equation, log BCF = 0.76 log K_{ow} - 0.23 (Lyman et al., 1982) and the values of log K_{ow} given in Section 1.2.1.1. This equation cannot differentiate BCF's if K_{ow} values are the same. The estimated log BCF values are 4.94, 4.94 and 6.25 for 2,3-dibromo-, 2,8-dibromo- and 2,3,7,8-tetrabromo-substituted compounds, respectively.

1.2.1.5. **SUMMARY OF ESTIMATED VALUES** -- The values for the parameters estimated from Leo's Fragmentation Theory and various regression equations are shown in Table 1-3. For the purpose of comparison, the corresponding values for dichlorodibenzo-p-dioxin and 2,3,7,8-TCDD are also given. It should be emphasized that, with the exception of the water solubility value for 2,3,7,8-TCDD, all other values for the chlorinated dibenzo-p-dioxins are estimated (NRCC, 1981, U.S. EPA, 1984a).

TABLE 1-3

Selected Parameters for Brominated and Chlorinated Dibenzo-p-dioxins Estimated from Predictive Theories

Compound	log K_{ow}	Solubility (µg/ℓ)	log K_{oc}	log BCF
2,3-Dibromo-	6.802	9	6.37	4.94
2,8-Dibromo-	6.802	11	6.37	4.94
2,3,7,8-Tetrabromo-	8.532	0.01	7.99	6.25
Dichloro-	4.71	6	4.60	3.30
2,3,7,8-Tetrachloro-	6.15	0.2	6.0	4.53 (3.30-4.48)*

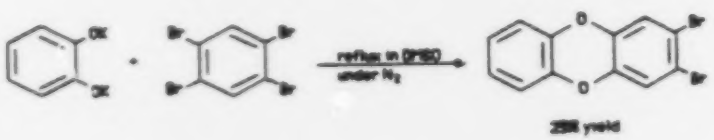
*The values given in parentheses are the range of experimentally determined BCF values (U.S. EPA, 1984a).

1.2.2. Chemical Properties. No information regarding the chemical properties of brominated dibenzo-p-dioxins is available in the literature as cited in the appendix; however, inferences about the chemical properties of these compounds can be made by analogy to the chlorinated dibenzo-p-dioxin compounds. (U.S. EPA, 1984a). Based on such analogy, it is likely that the tetrabromo-compound will be rather stable toward heated acids and alkalis. At temperatures of ~500°C, these compounds may begin to decompose. The brominated compounds may be susceptible to photoreductive dechlorination. Gamma radiation may also degrade the brominated compounds.

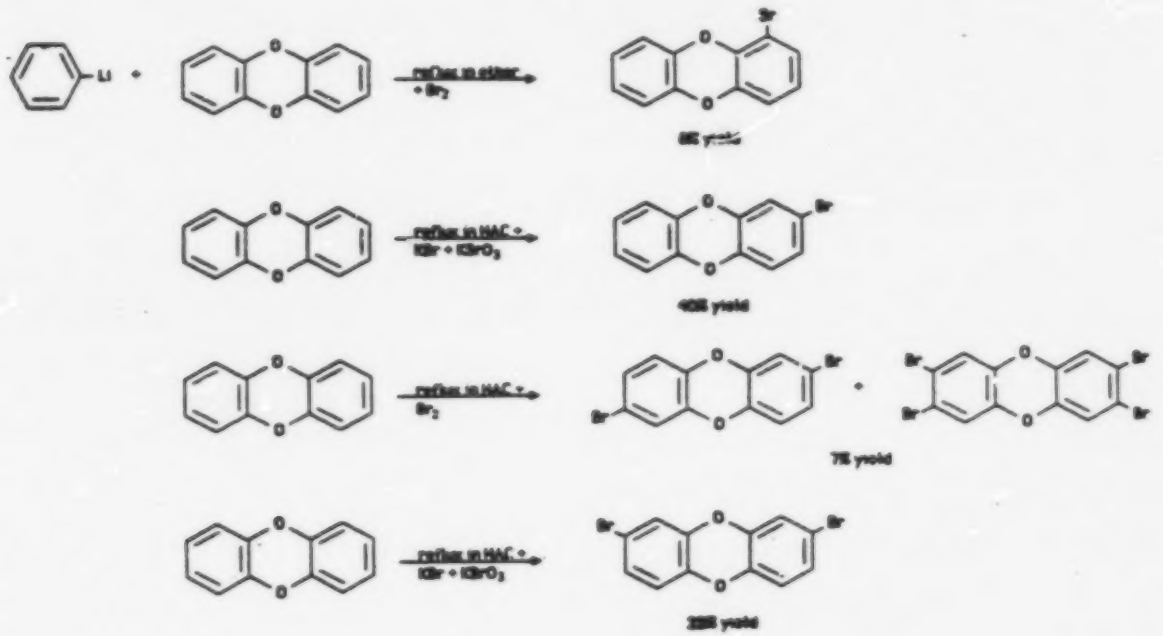
1.3. PRODUCTION DATA

None of the brominated dibenzo-p-dioxins are commercially manufactured in the United States. The presence of these compounds as impurities in other commercial products has not been reported in the literature some cited in Appendix. Although these compounds could be formed during the manufacture of bromophenols and combustion processes (i.e., municipal incineration) similar to polychlorinated dibenzo-p-dioxins, none of these compounds has been detected from combustion or other sources. A few of the brominated dibenzo-p-dioxins have been synthesized in the laboratory, the two most common methods for synthesis being condensation and substitution reactions.

1.3.1. Condensation Reaction. This reaction was used by Kende et al. (1974) to synthesize 2,3-dibromodibenzo-p-dioxin, by refluxing the dipotassium salt of catechol with 1,2,4,5-tetrabromobenzone in dimethyl sulfoxide under nitrogen according to the following reaction:



1.3.2. Substitution Reaction. The substitution reactions have been used (Kende et al., 1974; Gilman and Dietrich, 1957) for the synthesis of monobromo-, dibromo- and tetrabromodibenzo-p-dioxin according to the following reactions:



1.4. USE DATA

Although the formation of brominated dibenzo-p-dioxins is likely during the manufacture of brominated phenols (Chapter 3), these compounds have no commercial use.

2. ENVIRONMENTAL FATE AND TRANSPORT PROCESSES

Data pertinent to the environmental fate and transport of these compounds were not located in the available literature as cited in the appendix. Speculations regarding the environmental fate of these compounds are based on the estimated physical parameters given in Section 1.2. and the fate and transport of chlorinated dibenzo-p-dioxins discussed in U.S. EPA (1984a). In aquatic media, brominated dibenzo-p-dioxins may be resistant to biodegradation and may be photochemically stable in the absence of hydrogen donors. The estimated biodegradation half-life of 2,3,7,8-TCDD in aquatic media is >1 year (U.S. EPA, 1984a). Therefore, 2,3,7,8-tetrabromodibenzo-p-dioxin is likely to show a similar biodegradation half-life. Also, although 2,3,7,8-tetrabromodibenzo-p-dioxin may be normally resistant toward photolysis in aquatic media, photolysis may be significant in the presence of hydrogen atom donating substrate(s) and in the presence of such photosensitizers as algae present in surface waters. Like the corresponding chlorinated compounds (U.S. EPA, 1984a), lower brominated dibenzo-p-dioxins are expected to have a higher rate of photodegradation than the higher brominated compounds. Neither oxidation nor hydrolysis is likely to be a significant fate process for brominated dibenzo-p-dioxins. The volatilization rate of 2,3,7,8-TCDD from a pond was estimated to be 15-16 mg/year (U.S. EPA, 1984a). Therefore, 2,3,7,8-tetrabromodibenzo-p-dioxin, which has an estimated lower solubility in water and possibly lower vapor pressure than the corresponding chlorinated compound, is expected to volatilize from aquatic media at a similar rate. Based on the log K_{oc} and log BCF values given in Table 1-3 and by analogy from the chlorinated compounds (U.S. EPA, 1984a), sorption onto suspended particulate matter and sediment and bioconcentration in aquatic organisms will be important transport processes for

these compounds in aquatic media. In the case of 2,3,7,8-TCDD, >90% of the compound in an aquatic media was estimated to be present in the sorbed state (U.S. EPA, 1984a). As Table 1-3 indicates, both sorption and bioconcentration in aquatic media are expected to be higher for the brominated compounds than the corresponding chlorinated compounds. Among the brominated compounds, the tendency toward sorption and bioconcentration is expected to increase with the higher brominated compounds.

In the atmosphere, the brominated dibenzo-p-dioxins are likely to be present in the particle-sorbed phase. As is true for the corresponding chlorinated compounds (U.S. EPA, 1984a), photolysis of the surface layer of the particle-sorbed phase is likely. The primary removal mechanisms for atmospheric brominated dibenzo-p-dioxins are likely to be wet and dry deposition.

In soils, brominated dibenzo-p-dioxins may not undergo significant phototransformation or biotransformation. Like the corresponding chlorinated compound (U.S. EPA, 1984a), the biodegradation half-life of 2,3,7,8-tetrabromodibenzo-p-dioxin may be >10 years. Some evaporation from soil surfaces is likely, but these compounds are expected to sorb strongly to soil and persist in soil for long periods. Because of their expected low water solubility and high soil sorption capability under normal conditions, these compounds may not leach significantly from soil.

3. EXPOSURE

Pertinent data regarding the exposure to brominated Jibenzo-p-dioxins in air, water or food were not located in the available literatureas cited in the appendix. By analogy with the sources of chlorinated dibenzo-p-dioxins in the environment (U.S. EPA, 1984a), the likely sources of brominated dibenzo-p-dioxins in the environment are during the production of bromophenols, during incineration of selected industrial wastes, and possibly during municipal incineration. None of the brominated dibenzo-p-dioxins, however, has ever been reported in any environmental samples arising from these sources. The few primary manufacturers of di-, tri- and pentabromophenol in the United States are United-Guardian, Inc., Hauppauge, NY; Dow Chemical, Midland, MI; White Chemical Corp., Newark; NJ, and Great Lake Chemical Corp, El Dorado, AR (SRI, 1985). Since tetrabrominated and hexabrominated dibenzo-p-dioxins may be produced during the manufacture and incineration of tribromophenol and pentabromophenol, respectively (U.S. EPA, 1984a), these manufacturing sites should be investigated as the most likely environmental sources to contain detectable levels of dibenzo-p-dioxins.

4. PHARMACOKINETICS

4.1. ABSORPTION

Pertinent data regarding the absorption of the brominated dibenzo-p-dioxins were not located in the available literature as cited in the Appendix; however, absorption data are available from studies in laboratory animals of some members of the polychlorinated dibenzo-p-dioxins that have similar chemical and physical properties to the brominated compounds. Absorption efficiencies of 50-60% have been estimated for 2,3,7,8-TCDD when administered to rats in the diet (Fries and Marrow, 1975). Efficiency of absorption was 70-86% when the compound was administered by gavage to rats and hamsters in an oil vehicle (Rose et al., 1976; Piper et al., 1973; Olson et al., 1980). Poiger and Schlatter (1980) confirmed that the vehicle affected the gastrointestinal absorption of 2,3,7,8-TCDD. When 2,3,7,8-TCDD was administered in a suspension of soil or activated carbon, absorption efficiency was substantially decreased with levels as low as 0.07% for activated carbon. Similar effects were also reported for dermal absorption of 2,3,7,8-TCDD (Poiger and Schlatter, 1980). In rats dermal application of 2,3,7,8-TCDD in methanol resulted in absorption of ~40% of an equivalent oral dose while application in a soil/water paste resulted in absorption of ~2% of an equivalent oral dose. By analogy to 2,3,7,8-TCDD, it would be anticipated that 2,3,7,8-tetrabromodibenzo-p-dioxin would be absorbed similarly.

4.2. DISTRIBUTION

Bleavins et al. (1981) compared the tissue distribution of PCBs and PBBs in pregnant minks and ferrets. The animals were intraveneously administered the respective compounds as radiolabeled material. In the clams, higher levels of PBB than PCB were detected in the livers (5- to 10-fold), while

similar levels were observed in the kidneys. In adipose tissue, the concentration pattern was reversed with a 2- to 8-fold greater level of PCB as compared with PBB. The ratio of the mean concentration of PBB:PCB in amniotic fluid was 1:7 and 1:3 for the mink and ferrets, respectively. In the first trimester the mean PBB:PCB ratio was ~1:9.5 and 1:2.4 in minks and ferrets, respectively. In 2-week-old minks, however, the concentration of PBB was ~22.5-fold higher than PCB, reflecting a greater excretion of PBB in the maternal milk. The differences observed in this study may be related to the use of Aroclor 1242, which consists predominantly of lower chlorinated products as the source of the PCBs while a mixture of 2,4,5,2',4',5'- hexa- and 2,3,4,5,2',4',5'-heptabromobiphenyl was the PBB source. As a result of the differences observed in the distribution of PCBs, as compared with PBBs, it may be anticipated that some differences might occur in the distribution of the respective brominated and polychlorinated dibenzo-p-dioxins.

Other pertinent data regarding the distribution of the polybrominated dibenzo-p-dioxins were not located in the available literature as cited in the Appendix. The polychlorinated dibenzo-p-dioxin 2,3,7,8-TCDD has been demonstrated to distribute to liver and lipophilic tissues in rats, mice and hamsters following oral administration (Fries and Marrow, 1975; Rose et al. 1976; Piper et al., 1973; Kociba et al., 1978; Manara et al., 1982; Olson et al., 1980). In nonhuman primates however, adipose tissue and skin contained greater amounts of 2,3,7,8-TCDD than the liver (Van Miller et al., 1976).

The fetal toxicity of 2,3,7,8-TCDD has demonstrated that this compound is distributed to the fetus in laboratory rodents and nonhuman primates (Sections 5.3. and 5.4.). Nau et al. (1982) reported that the extent of distribution to the fetus sharply declined after placentation. In the early

fetus, 2,3,7,8-TCDD was distributed evenly throughout all tissues (Moore et al., 1976), while in later fetuses (17-21 days) preferential concentration in the liver was observed (Nau et al., 1982; Appelgren et al., 1983).

4.3. METABOLISM

Pertinent data regarding the metabolism of the brominated dibenzo-p-dioxins were not located in the available literature as cited in the Appendix. The corresponding polychlorinated dibenzo-p-dioxins were reported to be metabolized poorly (U.S. EPA, 1984a). *In vivo*, the polychlorinated dibenzo-p- dioxin metabolites consisted of dichlorinated mono- and dihydroxy derivatives that were present in either the free or conjugated form (Poiger et al., 1982; Sawahata et al., 1982; Tulp and Hutzinger, 1978). Interspecies variation in both quantitative and qualitative aspects of metabolism have been demonstrated in rats and hamsters using *in vivo* and *in vitro* assay systems. Poland and Glover (1979) and Guenthner et al. (1979) demonstrated that radiolabeled 2,3,7,8-TCDD bound to cellular macromolecules, microsomal protein and DNA, suggesting that at least small amounts of reactive metabolites were formed. The brominated dibenzo-p-dioxins are also likely to be metabolized poorly, although as with the polychlorinated derivative some of the metabolites may be reactive compounds of biological significance.

4.4. EXCRETION

Pertinent data regarding the excretion of the brominated dibenzo-p-dioxins were not located in the available literature as cited in the Appendix. The polychlorinated dibenzo-p-dioxin, 2,3,7,8-TCDD, is slowly eliminated from the body with elimination half-lives of 10.8-30.2 hours for the hamster and guinea pig, respectively (Olson et al., 1980; Gasiewicz and Neal, 1979). Olson and Bittner (1983) reported a slow second component to the elimination kinetics in rats with a $t_{1/2}$ of 75 days. The primary route of

excretion in the guinea pig, rat, mouse and monkey was in the feces, which accounted for 80-100% of the eliminated dose (U.S. EPA, 1984b). The hamster, the least sensitive species to 2,3,7,8-TCDD toxicity, excreted up to 41% of the eliminated dose in the urine (Olson et al., 1980). It would be expected that the brominated dibenzo-p-dioxins would also be eliminated slowly, predominantly by the fecal route and that they exhibit species variation regarding the route of elimination and the elimination half-life.

5. EFFECTS

5.1. CARCINOGENICITY

No studies of the potential carcinogenicity of the brominated dibenzo-p-dioxins per se were located in the available literature as cited in the Appendix, and these chemicals are not scheduled for testing by the NTP (1984).

A structurally related compound, 2,3,7,8-TCDD, has been tested for carcinogenicity in rats and mice. The chronic administration of 2,3,7,8-TCDD to rats by gavage (NTP, 1980a) resulted in increased incidences of hepatocellular carcinoma and squamous cell carcinoma of the hard palate while chronic administration in the diet (Kociba et al., 1978) resulted in squamous cell carcinoma of the lung and neoplastic nodule or carcinoma of the liver. In mice, chronic administration of 2,3,7,8-TCDD by gavage resulted in an increased incidence of hepatocellular carcinoma (NTP, 1980a). In addition, a mixture of two other congeners of polychlorinated dibenzo-p-dioxin (1,2,3,6,7,8- and 1,2,3,7,8,9-hexachlorodibenzo-p-dioxin) produced an increased incidence of liver cancer in mice and rats following chronic administration by gavage (NTP, 1980b). 2,7-Dichlorodibenzo-p-dioxin, another congener, failed to elicit a clear carcinogenic response when administered to mice and rats at high dietary levels of 5000 and 10,000 ppm (NTP, 1979). The male $B_6C_3F_1$ mice data suggest possible carcinogenic potential. By analogy, some congeners of the polychlorinated dibenzo-p-dioxins may be animal carcinogens. Given the structural specificity of the carcinogenic activity of the chlorinated dioxins, however, the effects of bromorather than chloro-substitution on potential carcinogenicity cannot be assessed until additional data are available.

5.2. MUTAGENICITY

Pertinent data regarding the mutagenicity of the brominated dibenzo-p-dioxins were not located in the available literature as cited in the Appendix. A similar compound, 2,3,7,8-TCDD, produced variable results using in vitro mutagenicity assays. Negative responses were generally observed in the reverse mutation assays using Salmonella typhimurium (U.S. EPA, 1984b), while positive responses were observed in a reverse mutation assay in Escherichia coli (Hussain et al., 1972), Saccharomyces cerevisiae (Bronzetti et al., 1983) and in the mouse lymphoma assay (Rogers et al., 1982). Metabolic activation was used only in the S. cerevisiae and some of the S. typhimurium assays. There is also little potential for 2,3,7,8-TCDD to cause chromosomal aberrations or react with DNA (U.S. EPA, 1984b); however, Poland and Glover (1979) detected small amounts of nonextractable radiolabel associated with liver DNA following i.p. administration to rats. The data from 2,3,7,8-TCDD suggest that the brominated dibenzo-p-dioxins will probably not produce positive responses in short-term assays to assess genotoxicity.

5.3. TERATOGENICITY

Pertinent data regarding the teratogenicity of the brominated dibenzo-p-dioxins were not located in the available literature as cited in the Appendix. The polychlorinated dibenzo-p-dioxin, 2,3,7,8-TCDD, has been demonstrated to be fetotoxic in the mouse, rat and rabbit (U.S. EPA, 1984b). The most common fetal defects were cleft palate and kidney anomalies. To investigate the teratogenic potential, there has also been a number of studies of human populations potentially exposed to 2,3,7,8-TCDD (U.S. EPA, 1984b). As a result of mixed results, some positive and some negative associations of birth defects with exposure, and serious confounders, such as exposure to other potentially active compounds, these

studies failed to either support or refute the teratogenic potential of 2,3,7,8-TCDD in humans. Considering the data on 2,3,7,8-TCDD it would be likely that some congeners of the brominated dibenzo-p-dioxins would demonstrate a teratogenic potential in laboratory animals.

5.4. OTHER REPRODUCTIVE EFFECTS

Pertinent data regarding the reproductive effects of the brominated dibenzo-p-dioxins were not located in the available literature as cited in the Appendix. The polychlorinated dibenzo-p-dioxin, 2,3,7,8-TCDD, has been demonstrated to be fetilcidal in monkeys that were maintained on diets containing ≥50 ppt of the compound for 7 months before mating and during gestation (Allen et al., 1979; Barsotti et al., 1979; Schantz et al., 1979). Fetotoxicity was also observed in laboratory rodents (U.S. EPA, 1984a). In addition, an unidentified congener of hexachlorodibenzo-p-dioxin was fetotoxic at a dose of 10 and 100 µg/kg administered on days 6-15 of gestation (Schwetz et al., 1973).

5.5. CHRONIC AND SUBCHRONIC TOXICITY

Pertinent data regarding the chronic or subchronic toxicity of the brominated dibenzo-p-dioxins were not located in the available literature as cited in the Appendix. Some members of a similar group of compounds, the polychlorinated dibenzo-p-dioxins, have been shown to be highly toxic in laboratory animals. In rats, chronic studies (oral exposure) indicate a NOEL of 0.001 µg/kg/day for liver damage (Kociba et al., 1978, 1979; NTP, 1980a). These studies also indicate that 0.05 µg/kg/day was a NOAEL and 0.1 µg/kg/day was a FEL. In mice, doses as low as 0.001 µg/kg/day produced amyloidosis (Toth et al., 1978, 1979) while doses of 0.001-0.006 µg/kg/day produced liver damage in the chronic NTP (1980a) study.

Nonhuman primates appeared also to be very sensitive to the toxic effects of 2,3,7,8-TCDD, demonstrating severe effects (e.g., hair loss, edema and pancytopenia) at exposure to dietary levels of 50 and 500 ppt for 9 months (Allen et al., 1977; Schantz et al., 1979). In these studies, the estimated total intake of 2,3,7,8-TCDD was 2-3 µg/kg bw (0.007-0.01 µg/kg/day).

A mixture of 1,2,3,6,7,8- and 1,2,3,7,8,9-hexachlorodibenzo-p-dioxin was highly toxic to rats and mice in a chronic (gavage) study (NTP, 1980b). The lower doses tested, 0.19 and 0.36 µg/kg/day for males and females, respectively, produced frank effects on the liver (described as toxic hepatitis). Another congener, 2,7-dichlorodibenzo-p-dioxin, however, was far less toxic to rats and mice in a chronic feeding study (NTP, 1979). At dietary exposures of 5000 and 10,000 ppm, the only effect observed was a decrease in body weight gain. The data from these three polychlorinated dibenzo-p-dioxins indicate a large variance in the degree of toxicity of the tested congeners in chronic studies and it is likely that the brominated analogs will also possess a similarly large variance.

5.6. OTHER RELEVANT INFORMATION

There are limited data regarding the acute and biochemical effects of some of the congeners of the polybrominated dibenzo-p-dioxins. It was suggested by Poland and Glover (1979) that many of the biological effects of the polyhalogenated dibenzo-p-dioxins are mediated by binding to cytosol receptors. Poland and Glover (1979) compared the binding affinities of various halogenated congeners of dibenzo-p-dioxin in C57BL/6J mice with the ability of these compounds to induce AHH activity in chicken embryos. The 2,3,7,8-tetrabromodibenzo-p-dioxin had approximately the same affinity for the cytosotic receptor as 2,3,7,8-TCDD (a comparison of relative induction of AHH was not performed). The 2,3,7-tribromodibenzo-p-dioxin, the only other brominated congener tested, had a relative binding affinity of 43% and

a relative biologic potency of 43%. The corresponding polychlorinated derivative, 2,3,7-trichlorodibenzo-p-dioxin, however, had a relative binding affinity and biologic potency of only 14 and 0.06%, respectively.

Poland and Glover (1973) and Poland et al. (1983) compared the induction of AHH activity between brominated and polychlorinated congeners of halogenated dibenzo-p-dioxins. Kende et al. (1974), using the chicken embryo assay, demonstrated that the 2,3,7,8-bromo- and chloro- congeners of the polyhalogenated dibenzo-p-dioxins induce AHH activity to an equally high degree, and that both the bromo- and chloro-1,2-dihalogenated dibenzo-p-dioxins failed to induce AHH activity. As observed previously, there was a marked difference in the AHH induction capability between the chloroand bromo- 2,3,7-trihalodibenzo-p-dioxins. In this study, the former was 2% and the latter 60% of the activity indicated by 2,3,7,8-TCDD. Nearly identical results were reported for the induction of δ-aminolevulinic acid synthetase by 2,3,7-tribromo- and 2,3,7-trichlorodibenzo-p-dioxin (Poland and Glover, 1973).

Similarly, Thunberg et al. (1984) reported nearly identical induction of AHH activity in male Sprague-Dawley rats administered either 2,3,7,8-tetrabromo- or 2,3,7,8-tetrachlorodibenzo-p-dioxin by gavage. Both compounds were given as a single dose of 10 μg/kg bw. Examination 4 weeks after treatment indicated that 2,3,7,8-tetrabromodibenzo-p-dioxin induced ~86% of the AHH activity as the polychlorinated analog. In this study liver UDP-glucuronosyltransferase activity was increased 5.4- and 3-fold and liver retinal concentration decreased 88 and 46% for 2,3,7,8-tetrachloro- and 2,3,7,8-tetrabromodibenzo-p-dioxin, respectively.

The only other study on the effect of a brominated dibenzo-p-dioxin was conducted in groups of 5-6 male Sprague-Dawley rats (Yang et al., 1983).

Rats were administered by gavage 25 µg/kg of either 2,3,7-tribromodibenzo-p-dioxin or 2,3,7,8-TCDD. Examination after 10 days revealed a decrease in comparison to control animals in the biliary excretion of ovuabain by 32.3 and 38.5% for the tetrachloroand tribromodibenzo-p-dioxin, respectively. In both groups, bile flow was decreased from 1.96 to 1.19 and 1.30 mg/min/g of liver in the control animal and the 2,3,7,8-TCDD and 2,3,7-tribromodibenzo-p-dioxin treated animals. Liver-to-body weight ratios were increased to ~149% of control value for both the bromo- and chloro- compound.

6. AQUATIC TOXICITY

Data regarding the toxic effects of the various brominated dibenzo-p-dioxins to aquatic organisms were not located in the available literature as cited in the Appendix; however, a limited amount of information on the toxic effects and residual concentration of polychlorinated dibenzo-p-dioxins was located. The qualitative effects of brominated dioxins may be similar to those of chlorinated dioxins, but no quantitative estimates of the toxic potency of brominated dioxins can be made from the following summary of the effects of chlorinated dioxins on aquatic species.

6.1. ACUTE TOXICITY

The effects of acute exposure to 2,3,7,8-TCDD have been reported for four species of freshwater fish and one species of amphibian (Table 6-1). In almost all of these studies, toxic effects were observed only after the acute exposure period ended. Miller et al. (1973, 1979) investigated the toxic effects of measured concentrations of 2,3,7,8-TCDD on juvenile coho salmon, Oncorhynchus kisutch, resulting from a 96-hour exposure. Upon completion of the exposure period, fish were transferred to clean flowing water for up to 114 days. Tests were conducted with two groups of fish that differed in initial mean weight. Food consumption, growth and survival of smaller fish were measured until 60 days after exposure and were found to be significantly reduced at 5.4 µg/kg bw (0.0056 µg/ℓ), but not at ≤0.54 µg/kg bw (0.00056 µg/ℓ). Growth and survival of larger fish were measured until 114 days after exposure and were significantly reduced at 5.4 µg/kg bw (0.0105 µg/ℓ) but not at ≤0.54 µg/kg bw (0.00105 µg/ℓ). The actual concentrations in fish and water were lower than the calculated values because much of the added 2,3,7,8-TCDD was adsorbed to the containers.

TABLE 6-1

Acute Toxicity of Chlorinated Dibenzo-p-dioxins to Aquatic Organisms

Species	Duration		LC_{50} (µg/l)	Effects	Reference
	Exposure (hours)	Test (days)			
Coho salmon *Oncorhynchus kisutch*	96	64	0.0056	Reduced growth, food consumption and survival	Miller et al., 1973, 1979
	96	114	0.0105	Reduced growth, food consumption, and survival	Miller et al., 1973, 1979
Rainbow trout (*Salmo gairdneri*)	96	72	NR	Temporary growth inhibition	Helder, 1981
eggs and larvae	96	164	NR	Teratologic effects, decreased survival and growth	Helder, 1981
juveniles	96	72	NR	Decreased survival and growth, histological effects	Helder, 1981
Guppy *Poecilia reticulatus*	120	37	NR	100% mortality by 37 days after beginning exposure	Miller et al., 1973; Norris and Miller, 1974
	24	69	NR	Higher incidence of fin necrosis	Miller et al., 1979
Northern pike *Esox lucius*	96	23	NR	Temporary inhibition of egg development	Helder, 1980
eggs and larvae	96	23	0.001	Decreased survival and growth	Helder, 1980
Frog (*Rana cadesbiana*) larvae	i.p. injection	50	NR	No effect on survival, metamorphosis and histology	Beatty et al., 1976
Adults	i.p. injection	35	NR	Temporary decrease in food consumption, but no effects on survival or histology	Beatty et al., 1976

NR = Not reported

The response of rainbow trout (Salmo gairdneri) eggs, larvae, and juveniles to exposure with 2,3,7,8-TCDD was investigated by Helder (1981). Newly fertilized eggs and juveniles were exposed for 96 hours to a range of nominal 2,3,7,8-TCDD concentrations (0.0001, 0.001 and 0.01, and 0.01 and 0.1 µg/ℓ, respectively) followed by transfer to clean water. There was no significant increase in egg mortality for rainbow trout up to the highest concentration of 0.01 µg/ℓ. Significantly greater mortality occurred after hatching and during yolk sac adsorption in both species at concentrations as low as 0.001 µg/ℓ. Total mortality of larvae was 26% at 0.01 µg/ℓ and 12% at 0.001 µg/ℓ. Although cumulative mortality was not significantly increased at the lowest test concentration (0.001 µg/ℓ), growth was significantly but temporarily retarded in larvae. Growth was significantly reduced in juveniles at both 0.1 and 0.01 µg/ℓ exposure concentrations over the 72-day observation period. At the highest concentration, mortality reached 100% by 27 days but at the lowest concentration mortality was 7% by 27 days.

Helder (1980) also exposed newly fertilized northern pike (Esox lucius) eggs to a range of nominal 2,3,7,8-TCDD concentrations (0.0001, 0.001 and 0.01 µg/ℓ) for 96 hours. After exposure, eggs were transferred to clean flowing water and response observations of eggs and fry were recorded throughout the following 19 days. There was no significant increase in egg mortality up to 0.01 µg/ℓ. Significantly greater mortality occurred after hatching and during yolk sac adsorption at concentrations as low as 0.001 µg/ℓ. Total mortality of fry reached 99% at 0.01 µg/ℓ and 50% at 0.001 µg/ℓ by 23 days after fertilization.

Miller et al. (1973) and Norris and Miller (1974) investigated the effects of exposing guppies, Poecilia reticulatus, to concentrations of 0.1,

1.0 and 10.0 µg/ℓ of 2,3,7,8-TCDD for 120 hours, followed by transfer to clean water. Some guppies (8-18%) reportedly died in each test concentration group during the exposure period. All treated fish died within 37 days after beginning exposure, with smaller fish generally dying first. Fin necrosis was reported in all fish surviving more than 10 days.

In a later study, Miller et al. (1979) measured the incidence of fin necrosis in guppies exposed for 24 hours to much lower concentrations of 2,3,7,8-TCDD and then maintained in clean water for 69 days. The incidence of fin necrosis was significantly greater in fish exposed to $\geq$0.0001 µg/ℓ than in controls or in fish exposed to 0.00001 µg/ℓ.

6.2. CHRONIC TOXICITY

The effects of chronic exposure to 2,3,7,8-TCDD have been reported for five species of freshwater invertebrates, three species of freshwater fish and one species of algae (Table 6-2). Yockim et al. (1978) investigated the responses of mosquitofish Gambusia affinis, channel catfish, Ictalurus punctatus, snails, Helosoma sp., water fleas, Daphnia magna and algae, Oedogonium cardiacum, exposed to measured mean daily concentrations of 2,3,7,8-TCDD at 0.0034 µg/ℓ in a recirculating aquatic model ecosystem. No effects over the 32-day exposure period were observed in snails, water fleas or algae as measured by reproductive activity, feeding and growth. Mortality of mosquitofish was recorded by day 14, and mean tissue concentration was 7.2 µg/kg bw. A second group of mosquitofish added at day 15 died after 15-20 days. Channel catfish added at day 32 all died after 15-20 days of exposure, and mean tissue concentration was 4.4 µg/kg bw. These results indicate that 15-20 days of exposure to ~0.003 µg/ℓ was lethal to fish, but had no effect on snails, water fleas and algae.

TABLE 6-2

Chronic Toxicity of 2,3,7,8-TCDD to Aquatic Organisms

Species	Duration		Lowest Effect Concentration	Method	Effect	Reference
	Exposure (hours)	Test (days)				
Mosquitofish (*Gambusia affinis*)	15	15	0.003 µg/L	Recirculating aquatic model ecosystem	100% mortality	Yockim et al., 1978
Channel catfish (*Ictalurus punctatus*)	20	20	0.003 mg/L	Recirculating aquatic model ecosystem	100% mortality	Yockim et al., 1978
Rainbow trout (*Salmo gairdneri*)	105	105	2300 µg/kg	In diet	Reduced survival, food consumption, and growth, increased fin erosion	Hawkes and Norris, 1977
Mosquito larvae (*Aedes aegypti*)	17	30	ND	NR	No effect on pupation	Miller et al., 1973
Oligochaete (*Paranais* sp.)	55	55	0.2	NR	Reduced reproduction	Miller et al., 1973
Snail *Physa* sp.	36	48	0.2	NR	Reduced reproduction	Miller et al., 1973
Helosoma sp.	32	46	ND	Recirculating aquatic model ecosystem	No apparent effects	Yockim et al., 1978
Water flea (*Daphnia magna*)	32	32	ND	Recirculating aquatic model ecosystem	No apparent effects	Yockim et al., 1978
Algae (*Oedogonium cardiacum*)	32	32	ND	Recirculating aquatic model ecosystem	No apparent effects	Yockim et al., 1978

NR = Not reported; NA = not applicable

Hawkes and Norris (1977) conducted chronic studies with groups of rainbow trout, Salmo gairdneri, fed diets containing 0.0023, 2.3 or 2300 µg/kg 2,3,7,8-TCDD, 6 days/week, for 15 weeks. The calculated doses were, respectively, 0.000032, 0.036 and 21.0 µg 2,3,7,8-TCDD/kg freeze dry bw/day. Consumption of food containing 0.0023 and 2.3 µg/kg had no effect on survival, food consumption, growth or fin morphology. Fish that were fed the highest dose showed reduced food consumption after 10 days, reduced growth by 7 days, fin erosion by 14 days, and mortality that began on day 33 reached 50% by day 61 and 88% by day 71.

Miller et al. (1973) exposed mosquitoes, Aedes aegypti, oligochaete worms, Paranais sp. and adult snails, Physa sp., to concentrations of 0.20 µg/ℓ of 2,3,7,8-TCDD for 17, 55 and 36 days, respectively. There was no significant difference in total pupation or pupation rate between exposed and control mosquito larvae during the 17-day exposure period or for the 30-day total test period. Exposure of oligocheate worms to 2,3,7,8-TCDD resulted in a significant decrease in the total number of worms at 55 days. Total and mean dry weight were also reduced, but the variation among replicates reduced the significance of this effect to p=0.057, indicating that 0.20 µg/ℓ exerted its principal effect on reproduction rather than individual worm growth. Exposure of adult snails to 0.20 µg/ℓ for 36 days had no significant effect on adult survival and egg production. The total snail hatch was ~30% lower (p=0.056) in the treated groups, but there was no significant difference in the percentage of survival of young snails.

6.3. PLANT EFFECTS

Zullei and Benecke (1978) conducted contact inhibition studies with the filamentous algae, Phormidium sp. Filter paper was spotted in three places with 1 µg of 2,3,7,8-TCDD. Disks (5 mm diameter) of filtered algae were

placed on the spots, and the filter paper was placed in a petri dish containing nutrient media. The motility of the algae filaments outward from the disks was measured over a 3-hour period with a photoelectric cell. Relative to controls, 1 µg of 2,3,7,8-TCDD caused significant inhibition of motility. Although the exposure concentration is unknown, these results indicate that this algal species may be affected by contact with contaminated substrates (i.e., sediment).

Data regarding the effects of brominated or chlorinated dibenzo-p-dioxins on aquatic plants were not located in the available literature as cited in the Appendix.

6.4. RESIDUES

No data on experimentally derived bioconcentration potentials or residual concentration of brominated or chlorinated dibenzo-p-dioxins were located in the available literature as cited in the Appendix; however, a number of investigators have reported concentrations of 2,3,7,8-TCDD in fish collected from the Great Lakes and the St. Lawrence Seaway drainage.

Levels of 2,3,7,8-TCDD in several species of commercial fish taken from eastern Lake Ontario, Lake Erie and the Welland Canal ranged from 0.002-0.039 µg/kg (Josephson, 1983). Rock bass, Ambloplites rupestris, showed no detectable levels. Highest concentrations generally occurred in American eels, Auguilla rustrata (0.006-0.039 µg/kg), followed by rainbow smelt, Osmerus mordax, and channel catfish, Ictalurus punctatus. The high fat content in these three species (37, 13 and 3.5%, respectively) may explain, in part, the higher 2,3,7,8-TCDD concentrations.

Levels ranging from 0.004-0.695 µg/kg were reported by the U.S. EPA (1984b) for axial muscle tissue of channel catfish, common carp, Cyprinus carpio, yellow perch, Perca flavescens, smallmouth bass, Micropterus

salmoides, sucker, Catastomidae, and lake trout, Salvelinus namaycush, from Tittabawasse, Grand and Saginaw Rivers, Lake Michigan and Saginaw Bay. The highest concentrations were detected in bottom feeding catfish and carp; the lowest concentrations were detected in smallmouth bass, yellow perch and suckers (Harless and Lewis, 1980).

7. EXISTING GUIDELINES AND STANDARDS

7.1. HUMAN

Pertinent guidelines and standards, including U.S. EPA ambient water and air quality criteria, drinking water standards, FAO/WHO ADIs, U.S. EPA or FDA Tolerances for raw agricultural commodities or foods, and ACGIH, NIOSH or OSHA occupational exposure limits for the brominated dibenzo-*p*-dioxins were not located in the available literature as cited in the Appendix.

7.2. AQUATIC

Guidelines and standards for the protection of aquatic organisms from the toxic effects of the brominated dibenzo-p-dioxins were not located in the available literature as cited in the Appendix.

8. RISK ASSESSMENT

No data were located on the carcinogenicity, mutagenicity, teratogenicity or chronic toxicity of any of the congeners of the brominated dibenzo-p-dioxins in the literature as cited in the appendix. The lack of appropriate data precludes the derivation of a q_1^* or an ADI.

There is information available on several congeners of a structurally similar group of compounds, the polychlorinated dibenzo-p-dioxins. Where data are available it is apparent that the individual congeners of the polychlorinated dibenzo-p-dioxins vary extensively with regard to biologic properties. The 2,3,7,8-TCDD congener has been demonstrated to be carcinogenic in rats and mice (NTP, 1980a; Kociba et al., 1978). Also a mixture of two isomers of hexachlorodibenzo-p-dioxin were positive in a carcinogenicity assay in rats and mice (NTP, 1980b), while the less chlorinated 2,7-dichlorodibenzo-p-dioxin failed to increase the tumor incidence in rats and mice maintained on diets containing high levels of the compound (NTP, 1979). The degree of chronic systemic toxicity for these congeners appears to parallel the observed carcinogenic response (see Section 5.5.). The chronic NOELs for 2,3,7,8-TCDD were $\leq$0.001 µg/kg/day and the chronic NOEL for the mixture of hexachlorodibenzo-p-dioxin was <0.19 µg/kg/day, while the NOAEL for 2,7-dichlorodibenzo-p-dioxin was ~250 µg/kg/day (assuming a rat consumes food equivalent to 0.05 of its body weight per day). In addition, the 2,3,7,8-TCDD congener produced terata in laboratory animals; however, data on other congeners were not available.

There are some data from short-term *in vitro* and *in vivo* studies which suggest that the brominated and chlorinated dibenzo-p-dioxins interact similarly with biologic systems. The ability of 2,3,7,8-TCDD and

2,3,7,8-tetrabromodibenzo-p-dioxin to bind to a cytosolic receptor protein, a step considered necessary for at least some of the biologic properties of these compounds, was nearly identical (Poland and Glover, 1979). In addition, the ability of both the 2,3,7,8-TCDD and tetrabromodibenzo-p-dioxins to induce AHH enzyme systems in the chicken embryo (Poland and Glover, 1973, 1979; Poland et al., 1983; Kende et al., 1974) and in vivo in rats (Thunberg et al., 1984) were similar. The correlation between receptor binding (Poland and Glover, 1979) and AHH induction (Poland and Glover, 1979; Kende et al., 1974) for 2,3,7-tribromo- and 2,3,7-trichlorodibenzo-p-dioxin was not as great. The relative receptor binding affinity of the brominated congener was ~3-fold greater than the chlorinated congener, while the relative ability to induce AHH activity was >500-fold greater. Another pair of congeners (the 1,2-dichloro- and 1,2-dibromodibenzo-p-dioxin) were totally inactive in both assay systems. The limited data base comparing the chlorinated and brominated dibenzo-p-dioxins indicates that in some instances the analogous congeners have similar biologic properties; however, the inconsistency in receptor binding and AHH induction of the 2,3,7-congeners demonstrates a need for caution in any extrapolations.

9. REPORTABLE QUANTITIES

9.1. REPORTABLE QUANTITY (RQ) RANKING BASED ON CHRONIC TOXICITY

Subchronic and chronic studies of the polybrominated dibenzo-p-dioxins were not located in the available literature as cited in the Appendix; therefore, derivation of an RQ is precluded (Table 9-1).

9.2. WEIGHT OF EVIDENCE AND POTENCY FACTOR ($F=1/ED_{10}$) FOR CARCINOGENICITY

Studies of the carcinogenic potential of the polybrominated dibenzo-p-dioxins were not located in the available literature as cited in the Appendix; therefore, the derivation of the potency factor is precluded. According to the IARC classification criteria, these compounds are Class 3 chemicals (i.e., this group of chemicals cannot be classified as to its carcinogenicity for humans). The Carcinogen Assessment Group of the U.S. EPA classifies these compounds as Group D compounds, the available data are inadequate to assess the carcinogenic potential (U.S. EPA, 1984c). It should be noted, however, that several related chlorinated dibenzo-p-dioxins, namely 2,3,7,8-TCDD and a mixture of the 1,2,3,6,7,8- and 1,2,3,7,8,9-hexachlorodibenzo-p-dioxins, have been shown to be animal carcinogens (U.S. EPA, 1984a). These compounds have increased the incidence of a variety of tumors in both rats and mice. In addition, there is some epidemiologic evidence that 2,3,7,8-TCDD is a human carcinogen.

TABLE 9-1

BROMINATED DIBENZO-P-DIOXINS

MINIMUM EFFECTIVE DOSE (MED) AND REPORTABLE QUANTITY (RQ)

Route:	
Dose:	
Effect:	
Reference:	
RV_d:	
RV_e:	
Composite Score:	
RQ:	Data are not sufficient for deriving an RQ.

BROMINATED DIBENZO-P-DIOXINS

10. REFERENCES

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APPENDIX

LITERATURE SEARCHED

This profile is based on data identified by computerized literature searches of the following:

CA SEARCH (Files 308, 309, 310, 311, 320
TOXLINE
RTECS
OHM TADS
STORET
SRC Environmental Fate Data Bases
SANSS
AQUIRE
TSCAPP

These searches were conducted in March, 1985. In addition, hand searches were made of Chemical Abstracts (Collective Indices 6 and 7), and the following secondary sources were reviewed:

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